



Bilirubin metabolism and Jaundice-1

By

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INTENDED LEARNING OBJECTIVES (ILOs)



By the end of this lecture the student will be able to:

- 1. Demonstrate the steps of heme catabolism**
- 2. Distinguish different types of jaundice**



Outlines

What are the steps of heme catabolism

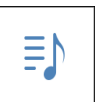
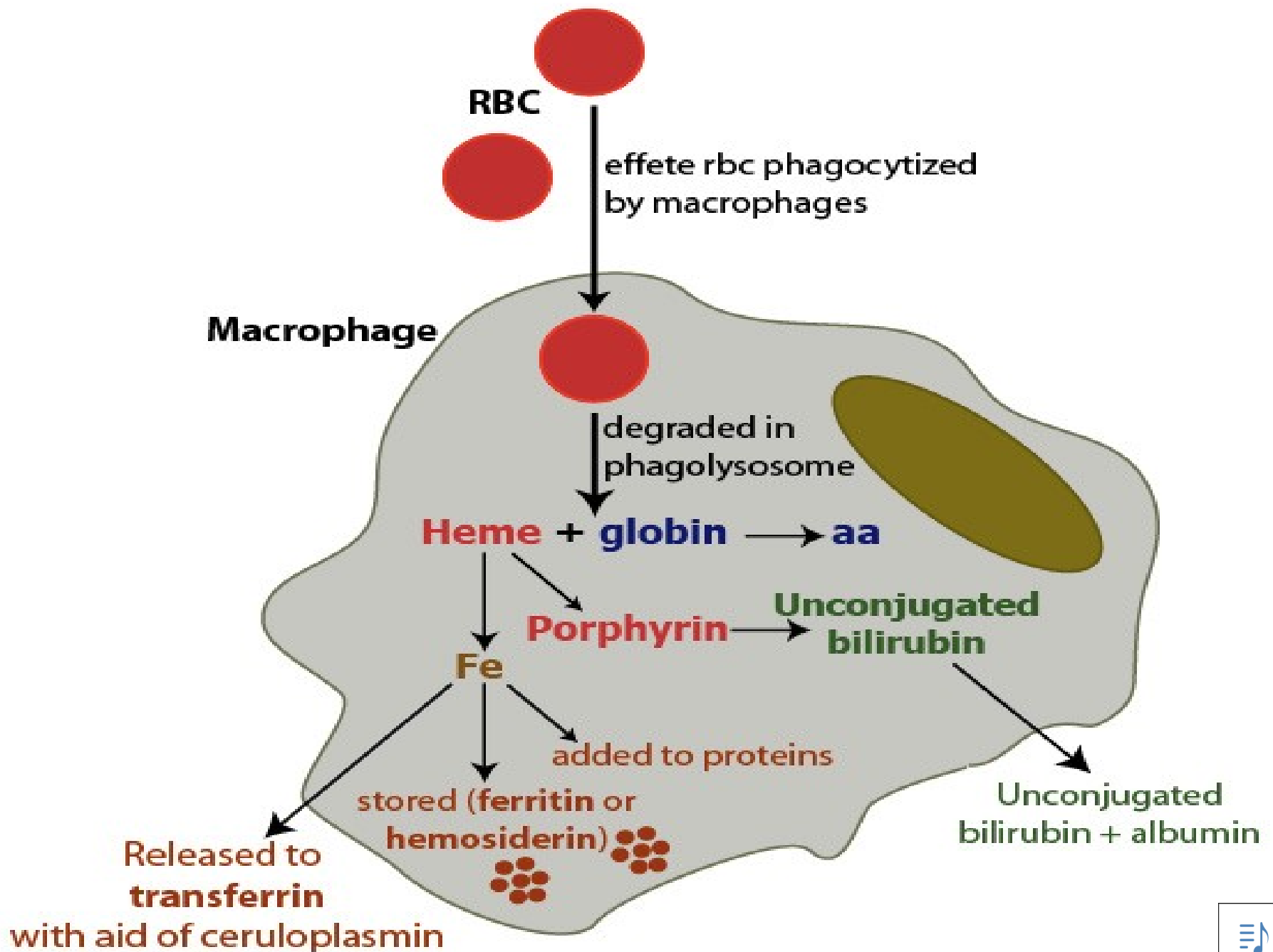
?What is Jaundice

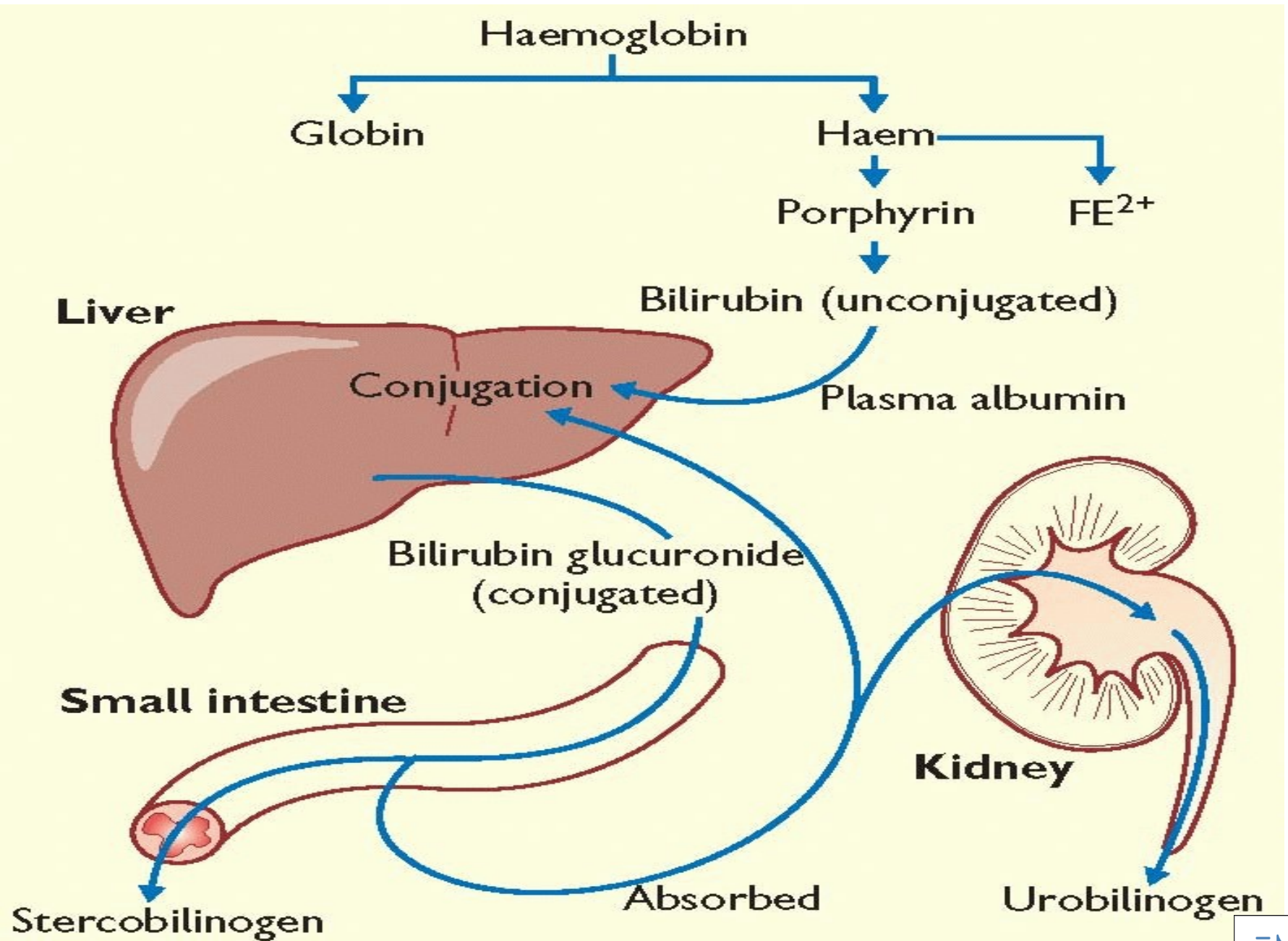
Catabolism of Heme

Human adults normally destroy about 200 billion erythrocytes per day.

After RBCs reach the end of their life span (average 120 days), they are phagocytosed by reticulo-endothelial cells of liver, spleen and bone marrow.







?What are the steps of heme catabolism

Steps of Heme catabolism

**Formation of .1
bilirubin**

**Uptake of bilirubin by the .2
liver**

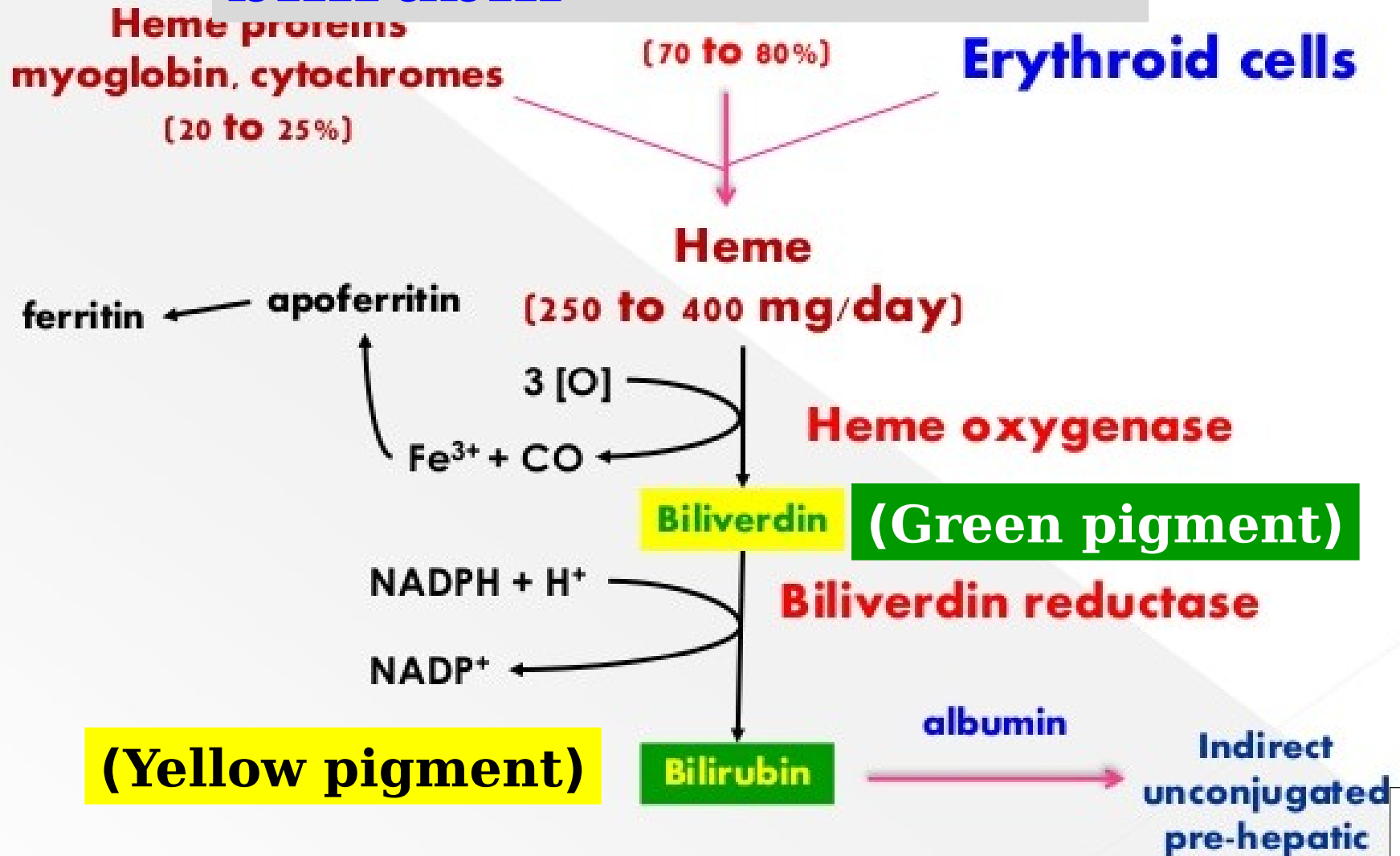
Formation of bilirubin diglucuronide .3

Secretion of bilirubin into bile .4

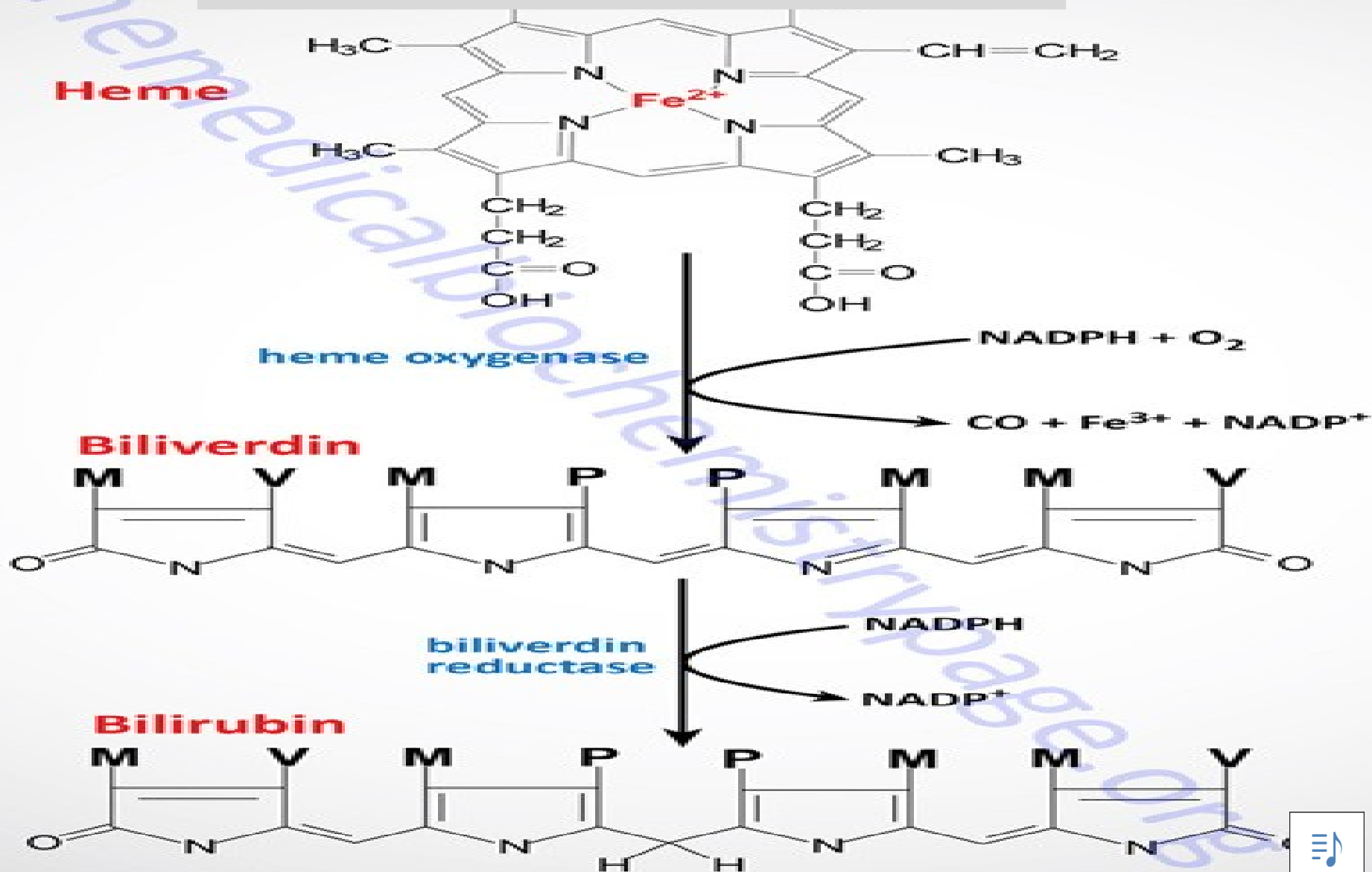
Formation of urobilins in the intestine .5



Formation of .1 bilirubin

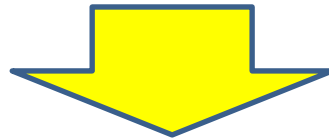


Formation of .1 bilirubin

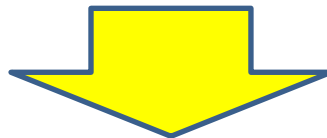


Formation of .1 bilirubin

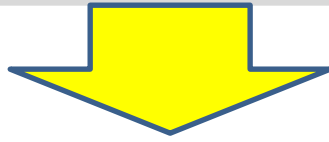
Heme catabolism is carried out in the microsomal **heme oxygenase system** of the reticuloendothelial cells



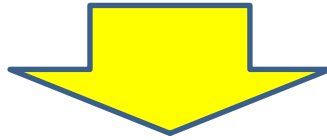
Opening of the porphyrin ring
converting cyclic heme to **linear biliverdin**
(**green** pigment)



Formation of .1 bilirubin



Iron is liberated from heme



In mammals, biliverdin is further **reduced to **bilirubin** (**yellow** pigment) by NADPH - dependent **biliverdin reductase** enzyme**



Uptake of bilirubin by the .2 liver

Bilirubin is slightly soluble in plasma. It transported to the liver bound to albumin forming unconjugated or indirect bilirubin

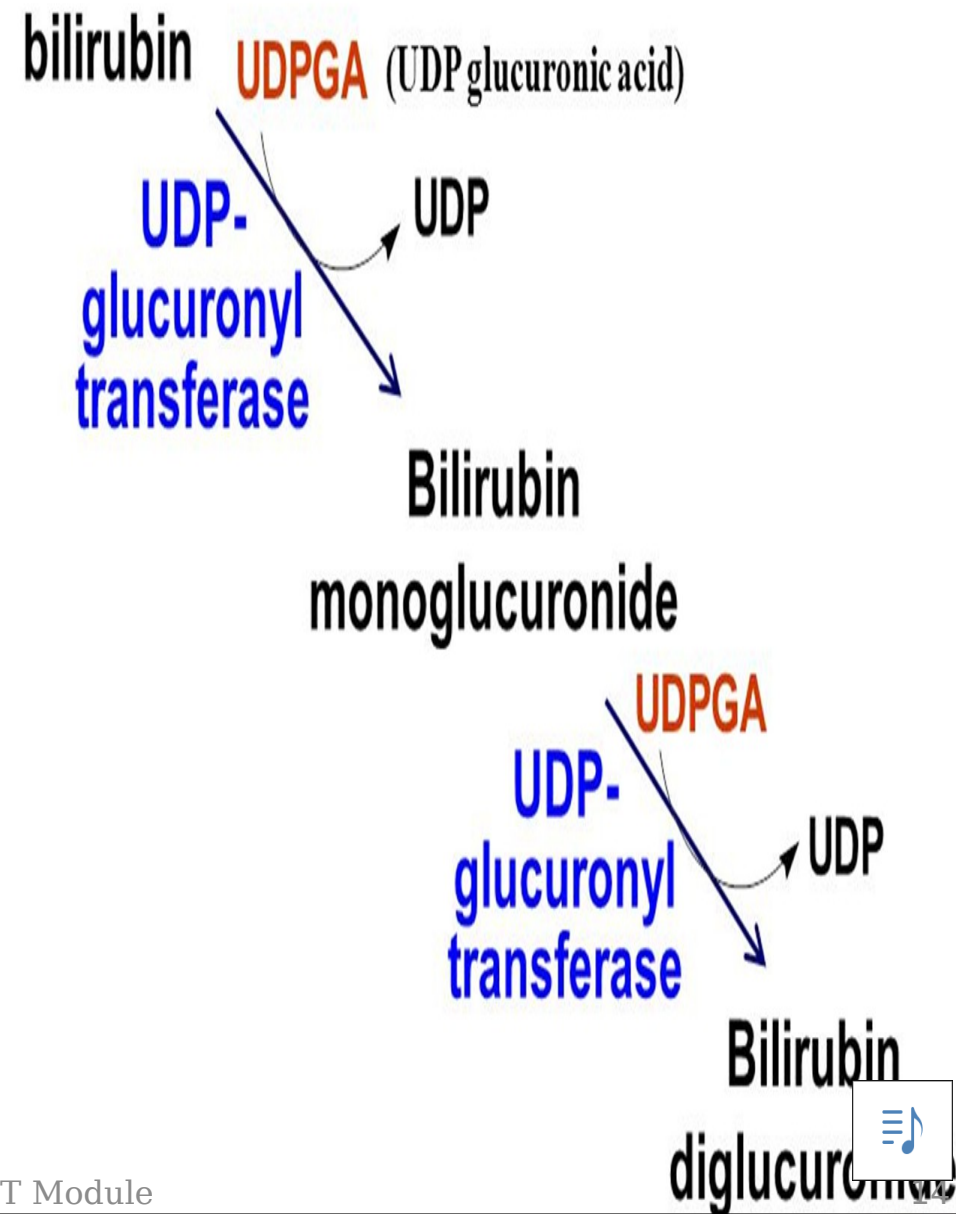
Liver uptake bilirubin by carrier mediated transport (facilitated transport)



Formation of bilirubin diglucuronide .3

Bilirubin
is converted to a
more polar
molecule by
conjugation with
two molecules of
glucuronic acid

This reaction is
catalyzed by
glucuronosyl
transferase
enzyme



Secretion of bilirubin into bile .4

Bilirubin diglucuronide (conjugated bilirubin)

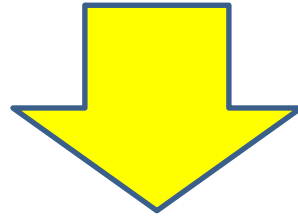
is actively transported against concentration gradient into the bile

Mostly, it is rate-limiting step for the entire process of hepatic bilirubin metabolism



Formation of urobilins in the intestine .5

Conjugated bilirubin is **hydrolyzed** and **reduced** by bacteria in the gut giving **urobilinogen**



Most of the urobilinogen is **oxidized** by intestinal bacteria to **stercobilin**, which gives **feces** the characteristic **brown** color

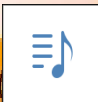
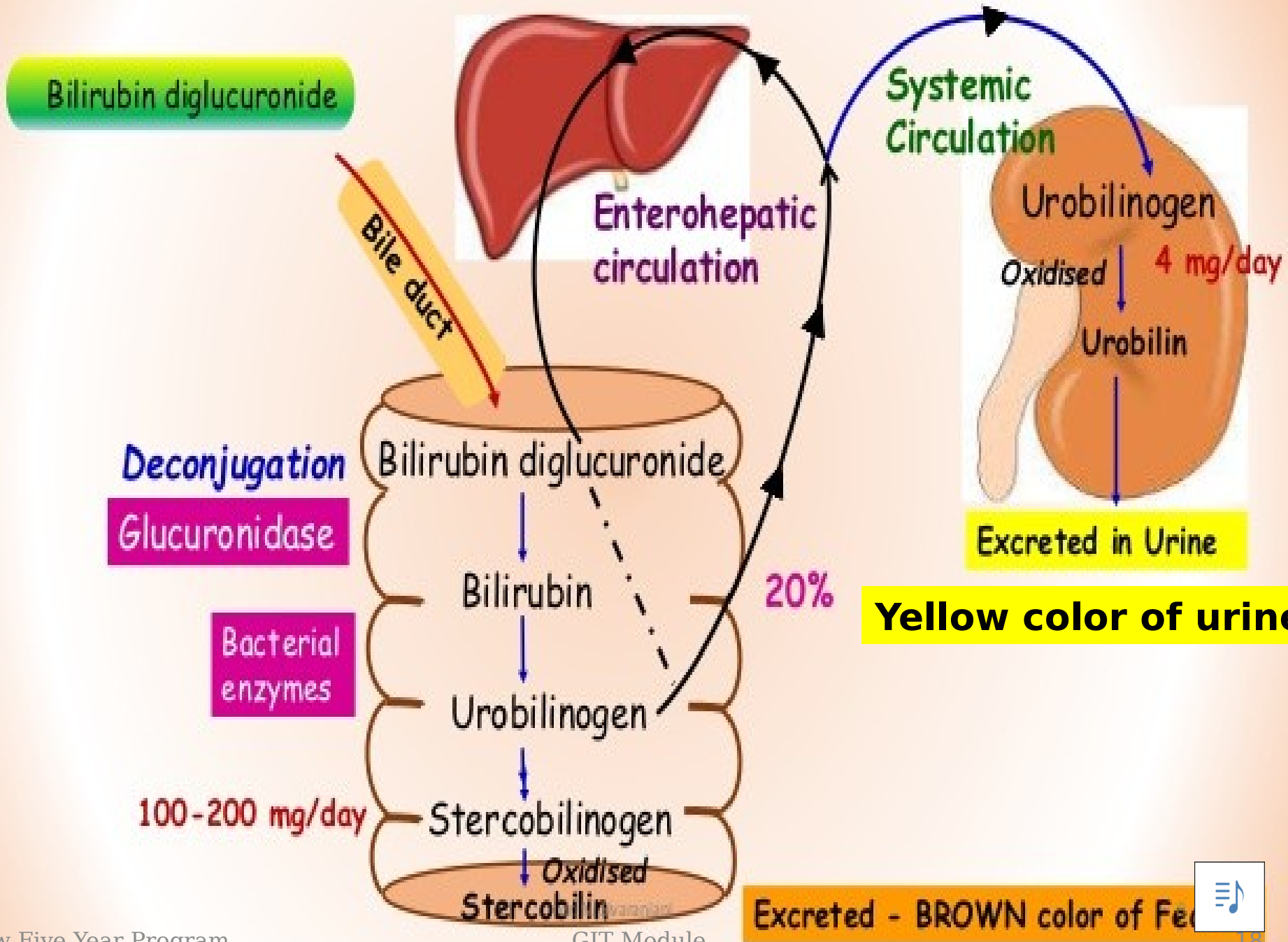


Formation of urobilins in the intestine .5

Some of the urobilinogen is **reabsorbed** from the gut and enters the portal blood and then **resecreted** into the **bile**

The rest of the urobilinogen is transported by the blood to the **kidney**, where it is converted to **yellow urobilin** and excreted, giving **urine** its characteristic **color**







?What is Jaundice



JAUNDICE



What is jaundice ?(icterus)



yellow color of skin, nail
beds, and sclerae
due by deposition of
bilirubin, secondary to
hyper-bilirubinemia

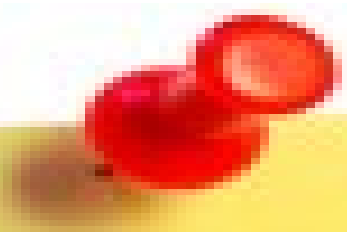


The normal plasma bilirubin level range from 0.3 - 1.2 mg/dl .

If the serum bilirubin exceeds 1 mg/dl
→ . hyperbilirubinemia

If the bilirubin level exceeds 2
→ g/dl, Jaundice will occur





Note: The **sclera** is particularly affected because it is **rich** in **elastin**, which has a **high affinity** for bilirubin





Note: unconjugated bilirubin can cross the blood-brain barrier into the central nervous system causing so encephalopathy .(kernicterus)

Alternatively, because of its water-solubility, only conjugated .bilirubin can appear in urine





:Note: Choluric jaundice
Choluria is the **presence** of bile pigments in the urine and occurs only in **conjugated** hyperbilirubinemia

:Acholuric jaundice
Is the **absence** of bile pigments in the urine and occurs only in **unconjugated** hyperbilirubinemia



MCQ

The substance deposited in skin and sclera in jaundice is:

- A. Biliverdin.**
- B. Only unconjugated bilirubin.**
- C. Only direct bilirubin.**
- ☒ D. Both bilirubin and bilirubin diglucuronide.**
- E. Hematin.**



Summary

- **After RBCs reach the end of their life span (average 120 days), they are phagocytosed by reticulo-endothelial cells of liver, spleen and bone marrow.**
- **Bilirubin is the end product of heme catabolism**
- **Jaundice is yellow color of skin, nail beds, and sclerae due by deposition of bilirubin, secondary to hyper-bilirubinemia**

Thank
you

Marwa Al

